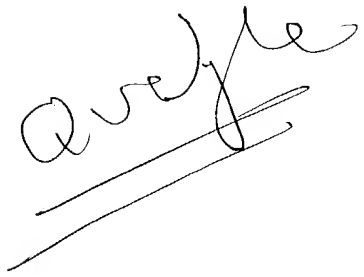
cyclohexyl, pyridyl, pyrimidinyl, pyrazinyl, oxopyridinyl, diazinyl, triazolyl, thienyl, oxazolyl, oxadiazolyl, thiazolyl, pyrrolyl, or furyl, optionally substituted. R3 is: H, hydroxy, lower-alkoxy, or lower-alkenyloxy; R4 is: H, lower-alkyl, lower-alkenyl, lower-alkoxy, hydroxy-lower-alkyl, lower-alkoxy-lower-alkyl, benzyl, oxo, or where R3 and R4 together are a bond, or as specified in the claims. Q is: ethylene, or is absent; X is: a bond, -O-, -S-, -CH-R11- (R11 defined in claims), -CHOR9- (R9 defined in claims), -OCO, -CO-, or C:NOR10- (R10 is carboxyalkyl, alkoxycarbonylalkyl, alkyl or H), with the bond emanating from an O or S atom joining to a saturated C atom of group Z or to R1; W is: -O-, or -S-; Z is: lower-alkylene, lower-alkenylene, hydroxy-lower-alkylidene, -O-, -S-, -O-Alk- (Alk is a lower alkylene), -S-Alk-, -Alk-O-, or -Alk-S. N is: 1, or 0 or 1 when X is -O-CO; and where m is 0 or 1; with provisos.

```
=> d his

     (FILE 'HOME' ENTERED AT 13:25:08 ON 28 FEB 2004)

     FILE 'REGISTRY' ENTERED AT 13:25:18 ON 28 FEB 2004
L1              STRUCTURE UPLOADED
L2           10 S L1 SSS FULL

     FILE 'CAPLUS' ENTERED AT 13:25:57 ON 28 FEB 2004
L3            8 S L2
L4          234 S ALZHEIMER AND PIPERAZINE
L5            0 S L3 AND L4
L6           14 S L4 AND PREVENTING
L7           21 S L4 AND PREVENTION
L8            4 S L4 AND PREVENTION AND PREVENTING AND DISEASE

=> s l3 and alzheimer
L9            0 L3 AND ALZHEIMER

=> s l3 and prevention and preventing a disease
L10           0 L3 AND PREVENTION AND PREVENTING A DISEASE
```



Welcome to STN International! Enter x:x

LOGINID:ssspta1611sxp

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	SEP 09	CA/CAplus records now contain indexing from 1907 to the present
NEWS 4	DEC 08	INPADOC: Legal Status data reloaded
NEWS 5	SEP 29	DISSABS now available on STN
NEWS 6	OCT 10	PCTFULL: Two new display fields added
NEWS 7	OCT 21	BIOSIS file reloaded and enhanced
NEWS 8	OCT 28	BIOSIS file segment of TOXCENTER reloaded and enhanced
NEWS 9	NOV 24	MSDS-CCOHS file reloaded
NEWS 10	DEC 08	CABA reloaded with left truncation
NEWS 11	DEC 08	IMS file names changed
NEWS 12	DEC 09	Experimental property data collected by CAS now available in REGISTRY
NEWS 13	DEC 09	STN Entry Date available for display in REGISTRY and CA/CAplus
NEWS 14	DEC 17	DGENE: Two new display fields added
NEWS 15	DEC 18	BIOTECHNO no longer updated
NEWS 16	DEC 19	CROPU no longer updated; subscriber discount no longer available
NEWS 17	DEC 22	Additional INPI reactions and pre-1907 documents added to CAS databases
NEWS 18	DEC 22	IFIPAT/IFIUDB/IFICDB reloaded with new data and search fields
NEWS 19	DEC 22	ABI-INFORM now available on STN
NEWS 20	JAN 27	Source of Registration (SR) information in REGISTRY updated and searchable
NEWS 21	JAN 27	A new search aid, the Company Name Thesaurus, available in CA/CAplus
NEWS 22	FEB 05	German (DE) application and patent publication number format changes

NEWS EXPRESS	DECEMBER 28 CURRENT WINDOWS VERSION IS V7.00, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 23 SEPTEMBER 2003
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may

result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 13:25:08 ON 28 FEB 2004

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 13:25:18 ON 28 FEB 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 27 FEB 2004 HIGHEST RN 655785-05-0
DICTIONARY FILE UPDATES: 27 FEB 2004 HIGHEST RN 655785-05-0

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

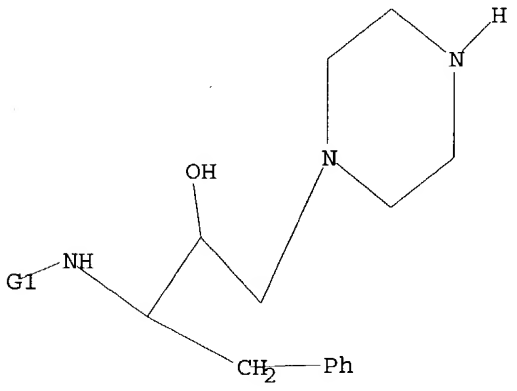
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading c:\program files\stnexp\queries\09895843.5

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



G1 H,Cb,Cy,Ak

Structure attributes must be viewed using STN Express query preparation.

```
=> s l1 sss full
FULL SEARCH INITIATED 13:25:50 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    498 TO ITERATE

100.0% PROCESSED     498 ITERATIONS                          10 ANSWERS
SEARCH TIME: 00.00.01

L2            10 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                               155.42     155.63

FILE 'CAPLUS' ENTERED AT 13:25:57 ON 28 FEB 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)
```



```
FILE COVERS 1907 - 28 Feb 2004  VOL 140 ISS 10
FILE LAST UPDATED: 27 Feb 2004  (20040227/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

=> s l2
L3            8 L2

=> d l3 fbib hitstr abs total

L3   ANSWER 1 OF 8  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2001:468210  CAPLUS
DN   135:61557
TI   Preparation of amino acid derivatives as retroviral protease inhibitors
IN   Chen, Xiaoqi; Kempf, Dale J.; Norbeck, Daniel W.
PA   Abbott Laboratories, USA
SO   U.S., 24 pp.
     CODEN: USXXAM
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
```

PI US 6251906 B1 20010626 US 1999-309141 19990510
US 1998-85709P P 19980515
US 2001008892 A1 20010719 US 2001-777282 20010206
US 1998-85709P P 19980515
US 1999-309141 A319990510

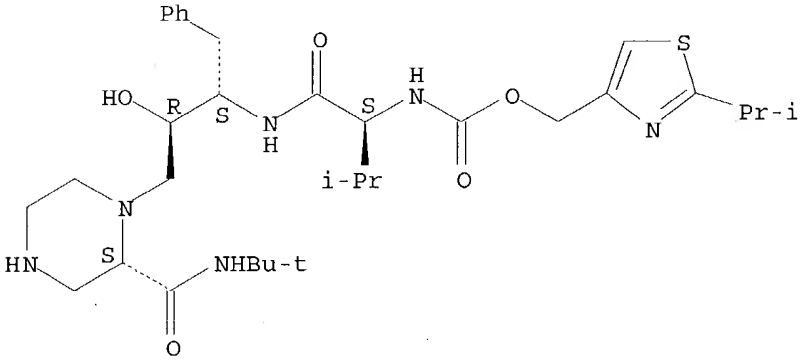
OS MARPAT 135:61557

IT **251105-64-3P 251105-79-0P 251112-24-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of amino acid derivs. as retroviral protease inhibitors)

RN 251105-64-3 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S,2R)-3-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-1-piperazinyl]-2-hydroxy-1-(phenylmethyl)propyl]amino]carbonyl]-2-methylpropyl]-, [2-(1-methylethyl)-4-thiazolyl]methyl ester (9CI) (CA INDEX NAME)

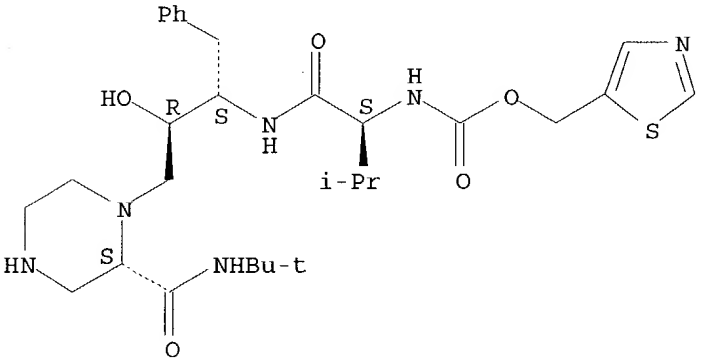
Absolute stereochemistry.



RN 251105-79-0 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S,2R)-3-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-1-piperazinyl]-2-hydroxy-1-(phenylmethyl)propyl]amino]carbonyl]-2-methylpropyl]-, 5-thiazolylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

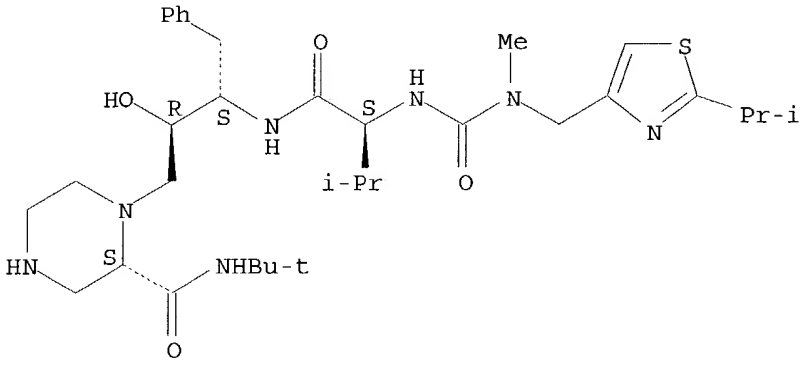


RN 251112-24-0 CAPLUS

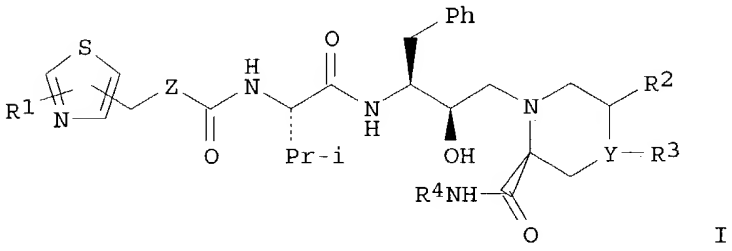
CN 2-Piperazinecarboxamide, N-(1,1-dimethylethyl)-1-[(2R,3S)-2-hydroxy-3-[[(2S)-3-methyl-2-[[[methyl[[2-(1-methylethyl)-4-

thiazolyl]methyl]amino]carbonyl]amino]-1-oxobutyl]amino]-4-phenylbutyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI



I

AB Amino acid derivs. I [R1 = H, alkyl, amino, alkylamino, dialkylamino, cycloalkyl; R2 = H, R3 = -WR5, where W is (CH2)0-6, O or S; Y = N or CH (with provisos) and R5 = alkyl or aryl; or R2R3 = (CH2)4; R4 = H, alkyl, cycloalkyl, aryl, (aryl)alkyl, heterocyclyl, (heterocyclyl)alkyl, heteroaryl, or (heteroaryl)alkyl; Z = O, S, CH2, (un)substituted imino] were prepared as retroviral proteases inhibitors, in particular for inhibiting human immunodeficiency virus (HIV) protease. Thus, 2-(1-methylethyl)-4-thiazolylmethyl [(1S)-1-[[[(1S,2R)-3-[(2S)-4-(1,3-benzodioxol-5-ylmethyl)-2-[[(1,1-dimethylethyl)amino]carbonyl]-1-piperazinyl]-2-hydroxy-1-(phenylmethyl)propyl]amino]carbonyl]-2-methylpropyl]carbamate was prepared and showed 60% inhibition of HIV protease at 0.5 nM concentration

RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

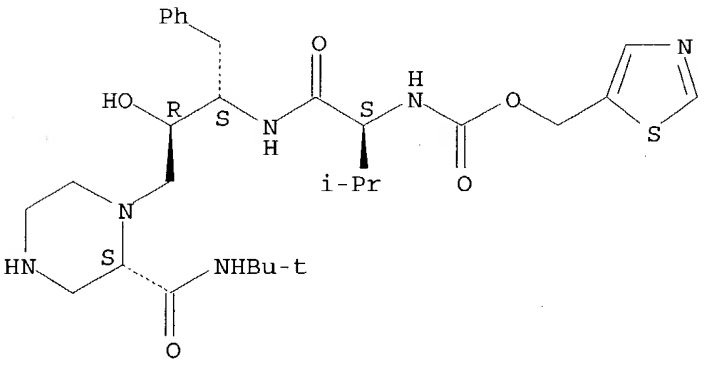
L3 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:753234 CAPLUS
DN 132:3551
TI Preparation of amino acid derivatives as retroviral protease inhibitors
IN Chen, Xiaoqi; Kempf, Dale J.; Norbeck, Daniel W.; Mohammadi, Fariborz
PA Abbott Laboratories, USA
SO PCT Int. Appl., 81 pp.

CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9959994	A1	19991125	WO 1999-US10130	19990507
	W: CA, JP, MX				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
				US 1998-80028 A	19980515
	CA 2331756	AA	19991125	CA 1999-2331756	19990507
				US 1998-80028 A	19980515
				WO 1999-US10130W	19990507
	EP 1077977	A1	20010228	EP 1999-920411	19990507
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
				US 1998-80028 A	19980515
				WO 1999-US10130W	19990507
	JP 2002515501	T2	20020528	JP 2000-549612	19990507
				US 1998-80028 A	19980515
				WO 1999-US10130W	19990507

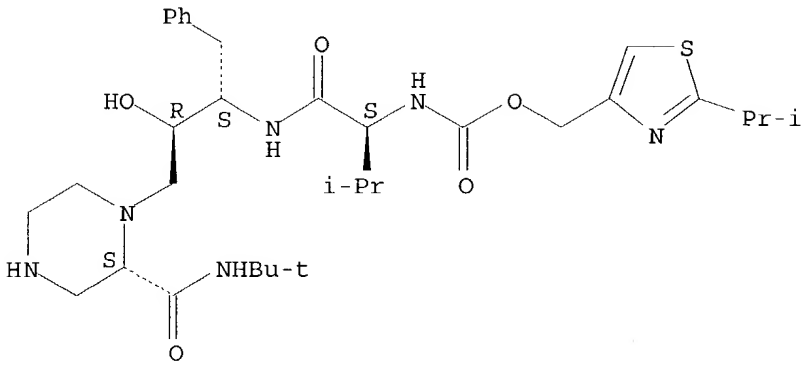
OS MARPAT 132:3551
IT **251105-79-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of amino acid derivs. as retroviral protease inhibitors)
RN 251105-79-0 CAPLUS
CN Carbamic acid, [(1S)-1-[[[(1S,2R)-3-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-1-piperazinyl]-2-hydroxy-1-(phenylmethyl)propyl]amino]carbonyl]-2-methylpropyl]-, 5-thiazolylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



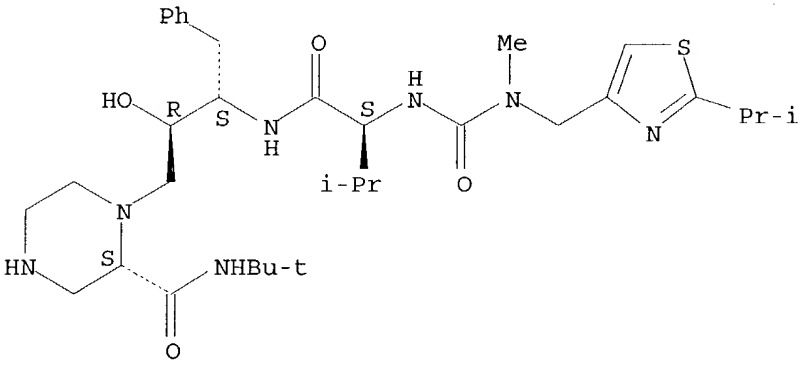
IT **251105-64-3P 251112-24-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of amino acid derivs. as retroviral protease inhibitors)
RN 251105-64-3 CAPLUS
CN Carbamic acid, [(1S)-1-[[[(1S,2R)-3-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-1-piperazinyl]-2-hydroxy-1-(phenylmethyl)propyl]amino]carbonyl]-2-methylpropyl]-, [2-(1-methylethyl)-4-thiazolyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

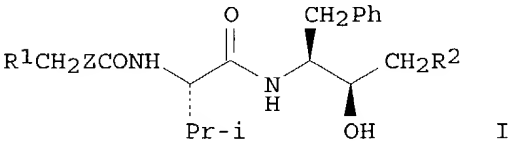


RN 251112-24-0 CAPLUS
CN 2-Piperazinecarboxamide, N-(1,1-dimethylethyl)-1-[(2R,3S)-2-hydroxy-3-[[(2S)-3-methyl-2-[[[methyl[[2-(1-methylethyl)-4-thiazolyl]methyl]amino]carbonyl]amino]-1-oxobutyl]amino]-4-phenylbutyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI

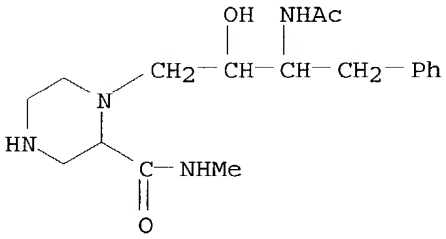


AB Compds. I [R1 = thiazolyl or alkyl-, amino-, alkylamino, dialkylamino, or cycloalkyl-substituted thiazolyl; R2 = 4-substituted 2-(un)substituted carbamoylpiperidino or -piperazin-1-yl; Z = O, S, CH2, NR7, where R7 = H or (un)substituted alkyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl] were prepared as inhibitors of retroviral proteases, in particular human immunodeficiency virus (HIV) protease. Thus, 2-(1-methylethyl)-4-thiazolylmethyl [(1S)-1-[[[(1S,2R)-3-[(2S)-4-(1,3-benzodioxol-5-ylmethyl)-2-[[(1,1-dimethylethyl)amino]carbonyl]-1-piperazinyl]-2-hydroxy-1-

(phenylmethyl)propyl]amino]carbonyl]-2-methylpropyl]carbamate was prepared and assayed for inhibition of HIV protease (60% at 0.5 nM) and antiviral activity (EC50 = 3 nM and LC50 = 12.76 μM).

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:476011 CAPLUS
DN 125:184889
TI The design, modeling and evaluation of potential HIV protease inhibitors using BLITZ, an interactive computer graphics working tool
AU Mahmoudian, M.; Laczkowski, A.; Karrer, A.; Swanson, S. M.; Meyer, E. F. Jr.
CS Department of Pharmacology, University of Medical Sciences, Teheran, Iran
SO Journal of Sciences, Islamic Republic of Iran (1996), 7(1), 8-12
CODEN: JSIIEN; ISSN: 1016-1104
PB National Center for Scientific Research
DT Journal
LA English
IT **180911-02-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(design and modeling and evaluation of potential HIV protease inhibitors using interactive computer graphics working tool BLITZ in relation to AIDS treatment)
RN 180911-02-8 CAPLUS
CN 2-Piperazinecarboxamide, 1-[3-(acetylamino)-2-hydroxy-4-phenylbutyl]-N-methyl- (9CI) (CA INDEX NAME)



AB Several nonpeptide small mols. were designed as potential inhibitors of HIV protease and their structures were constructed by computer-aided mol. modeling and docked into the active site of HIV protease. Models of the complexes of inhibitors and the HIV protease were refined using nonbonded and H-bonding terms. The refined energy of selected complexes showed that the designed inhibitors fitted tightly into the active site of receptor cavity. The structure of the designed inhibitor (HI-082) was superimposed on the mol. of haloperidol (which has been reported to have anti-HIV protease activity) and it was found that they share a number of common structural features. These results showed that these small nonpeptide mols. interact strongly with the HIV protease and may therefore inhibit its action in which case they would be potential anti-AIDS agents.

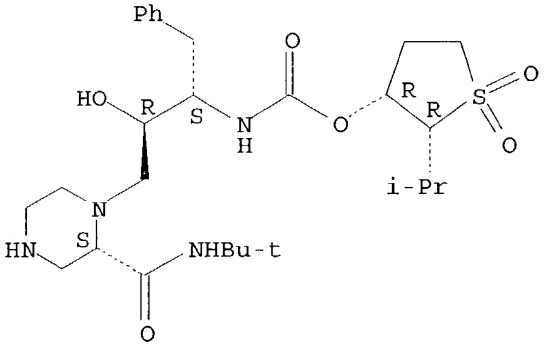
L3 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:367737 CAPLUS
DN 125:58548
TI Piperazinecarboxamide derivative HIV protease inhibitors useful for the

treatment of AIDS
IN Kim, Byeong Moon; Vacca, Joseph P.
PA Merck and Co., Inc., USA
SO Brit. UK Pat. Appl., 53 pp.
CODEN: BAXXDU
DT Patent
LA English
FAN.CNT 1

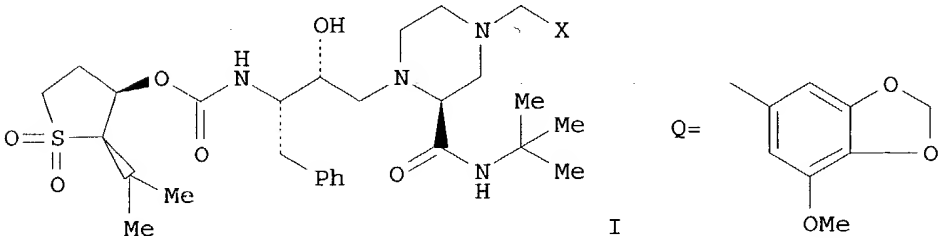
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI GB 2292146	A1	19960214	GB 1995-15802	19950801
			US 1994-289477	19940811
US 5650412	A	19970722	US 1995-548415	19951026
			US 1994-289477	19940811

OS MARPAT 125:58548
IT **165879-79-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of piperazinecarboxamide derivs. as HIV protease inhibitors)
RN 165879-79-8 CAPLUS
CN Carbamic acid, [3-[2-[[(1,1-dimethylethyl)amino]carbonyl]-1-piperazinyl]-2-hydroxy-1-(phenylmethyl)propyl]-, tetrahydro-2-(1-methylethyl)-1,1-dioxido-3-thienyl ester, [2R-[2α,3α[1S*,2R*,3(S*)]]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI



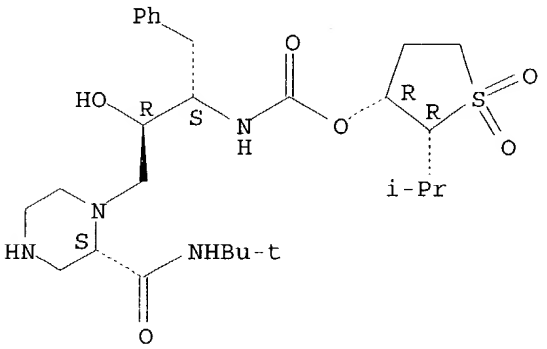
I

Q=

AB Title compds. I [X = stable 8- to 10-membered bicyclic heterocycle, any ring of which may be saturated or unsatd., and which consists of C atoms and 1-3 heteroatoms selected from N, S, and O, with said heterocycle (un)substituted with OH, halo, C1-4 alkyl, C1-4 alkoxy, or oxo; with proviso that X ≠ thieno[2,3-b]thien-2-yl or quinolinyl], and pharmaceutically acceptable salts thereof, are useful as HIV protease inhibitors. For example, the preferred compound I [X = Q] (II) was prepared in 68% yield by reductive alkylation of the corresponding piperazine derivative [multi-step preparation given] with 3-methoxy-4,5-methylenedioxybenzaldehyde and NaBH(OAc3). In a cell-spread assay using MT-4 lymphoid cells infected with wild-type HIV-1, II had CIC95 of 25 nM.

L3 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:857593 CAPLUS
DN 124:86938
TI Substituted alkylpyridines as P3' ligands for the hydroxyethylpiperazine class of HIV-1 protease inhibitors: improved pharmacokinetic profiles
AU Kim, B. Moon; Hanifin, Colleen M.; Zartman, C. Blair; Vacca, Joseph P.; Michelson, Stuart R.; Lin, Jiunn H.; Chen, I.-W.; Vastag, Kari; Darke, Paul L.; et al.
CS Department of Medical Chemistry, Merck Research Laboratories, West Point, PA, 19486, USA
SO Bioorganic & Medicinal Chemistry Letters (1995), 5(19), 2239-44
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier
DT Journal
LA English
IT **165879-79-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
{[[[(alkylamino)carbonyl]piperazinyl]hydroxyalkyl]carbamic acid thienyl ester S,S-dioxide derivs. as HIV inhibitors)
RN 165879-79-8 CAPLUS
CN Carbamic acid, [3-[2-[[(1,1-dimethylethyl)amino]carbonyl]-1-piperazinyl]-2-hydroxy-1-(phenylmethyl)propyl]-, tetrahydro-2-(1-methylethyl)-1,1-dioxido-3-thienyl ester, [2R-[2α,3α[1S*,2R*,3(S*)]]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB As a systematic approach to develop HIV-1 protease inhibitors exhibiting desirable pharmacokinetic profiles, hydroxyethylpiperazine series of inhibitors containing various mono- or dialkyl-substituted pyridylmethyl groups have been examined Very high enzyme inhibitory potency and antiviral

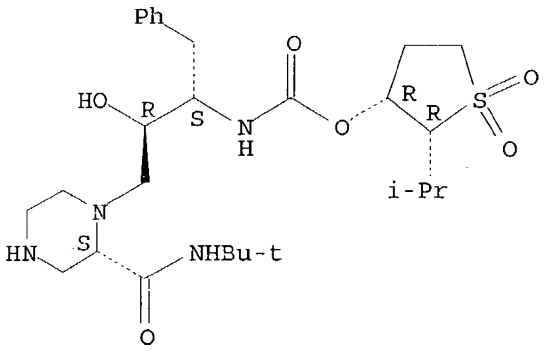
activity in a whole cell assay were observed with these inhibitors and, when administered orally to dogs, selected compds. in this series exhibited prolonged half-lives compared to the non-substituted pyridylmethyl compound, i.e., [2R-[2α,3α[1S*,2R*,3(S*)]]]-[3-[2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(4-pyridinylmethyl)-1-piperazinyl]-2-hydroxy-1-(phenylmethyl)propyl]carbamic acid tetrahydro-2-(1-methylethyl)-3-thienyl ester S,S-dioxide.

L3 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:711972 CAPLUS
DN 123:112077
TI Preparation of piperazine derivatives as HIV protease inhibitors
IN Kim, Byeong Moon; Vacca, Joseph P.; Ghosh, Arun K.; Guare, James P., Jr.; Huff, Joel R.; Hungate, Randall W.; Lee, Hee Yoon; Thompson, Wayne J.
PA Merck and Co., Inc., USA
SO PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9418192	A1	19940818	WO 1994-US1370	19940207
	W: AU, BB, BG, BR, BY, CA, CN, CZ, FI, HU, JP, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, UZ				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
				US 1993-17090	19930212
	AU 9461352	A1	19940829	AU 1994-61352	19940207
				US 1993-17090	19930212
				WO 1994-US1370	19940207

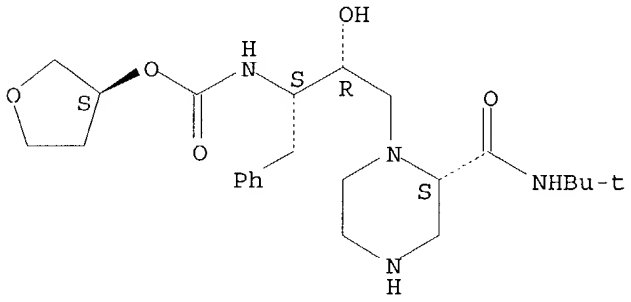
OS MARPAT 123:112077
IT **165879-79-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazine derivs. as HIV protease inhibitors)
RN 165879-79-8 CAPLUS
CN Carbamic acid, [3-[2-[[(1,1-dimethylethyl)amino]carbonyl]-1-piperazinyl]-2-hydroxy-1-(phenylmethyl)propyl]-, tetrahydro-2-(1-methylethyl)-1,1-dioxido-3-thienyl ester, [2R-[2α,3α[1S*,2R*,3(S*)]]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

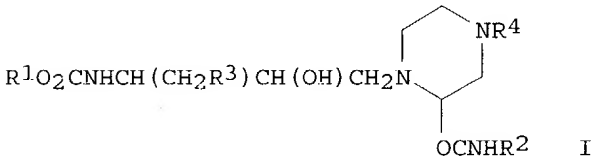


IT **159462-59-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of piperazine derivs. as HIV protease inhibitors)
RN 159462-59-6 CAPLUS
CN Carbamic acid, [3-[2-[[(1,1-dimethylethyl)amino]carbonyl]-1-piperazinyl]-2-hydroxy-1-(phenylmethyl)propyl]-, tetrahydro-3-furanyl ester, [2S-[1[1R*(R*),2S*],2R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI



I

AB Title compds. I (R1 = 5-7-membered carbocyclyl, 5-7-membered heterocyclyl; R2 = C1-5 alkyl, 5-7-membered carbocyclyl; R3 = Ph, C5-7 cycloalkyl; R4 = CO2, SO3, 5-7-membered heterocyclyl, C1-4 alkenyl, C3-5 cycloalkyl, etc.) or a salt thereof, useful for treating infection of HIV and AIDS, are prepared To N-tert-butyl-1-[3'(S)-[3"(S)-tetrahydrofuranyloxycarbonylamino]-2'-(R)-hydroxy-4'-phenylbutyl]piperazine-2(S)-carboxamide and 3-hydroxybenzaldehyde in MeOH were added NaBH3CN and AcOH to give title compound N-tert-butyl1-[3'(S)-[3"(S)-tetrahydrofuranyloxycarbonylamino]-2'(R)-hydroxy-4'-phenylbutyl]-4-(3'-hydroxyphenylmethyl)piperazine-2(S)-carboxamide which inhibited microbial expressed HIV protease with IC50 0.1-10 nM.

L3 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:120890 CAPLUS
DN 122:150813
TI A new hydroxyethylamine class of HIV-1 protease inhibitors with high antiviral potency and oral bioavailability
AU Kim, B. Moon; Vacca, Joseph P.; Guare, James P.; Hanifin, Colleen; Michelson, Stuart R.; Darke, Paul L.; Zugay, Joan A.; Emini, Emilio A.; Schleif, William; et al.
CS Dep. Medicinal Chem., Merck Research Labs., West Point, PA, 19486, USA
SO Bioorganic & Medicinal Chemistry Letters (1994), 4(19), 2273-8
CODEN: BMCLE8; ISSN: 0960-894X
DT Journal

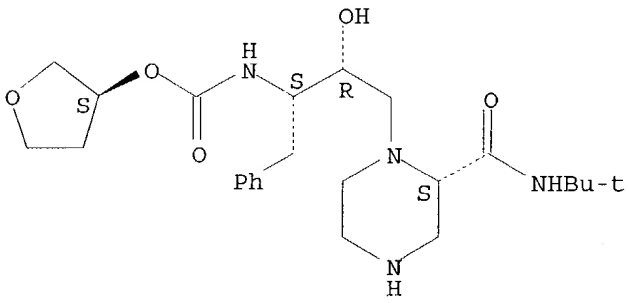
LA English

IT **159462-59-6P 159462-81-4P 159462-82-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(structure of hydroxyethylamine class of HIV-1 protease inhibitors with high antiviral potency and oral bioavailability)

RN 159462-59-6 CAPLUS

CN Carbamic acid, [3-[2-[[(1,1-dimethylethyl)amino]carbonyl]-1-piperazinyl]-2-hydroxy-1-(phenylmethyl)propyl]-, tetrahydro-3-furanyl ester, [2S-[1[1R*(R*),2S*],2R*]]- (9CI) (CA INDEX NAME)

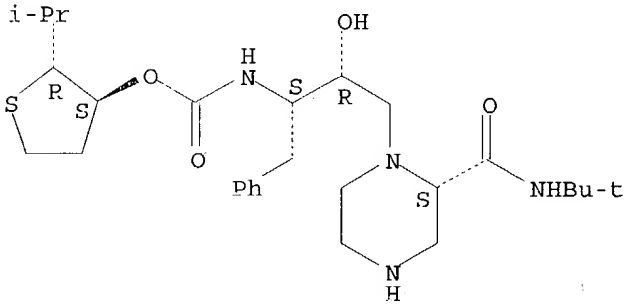
Absolute stereochemistry.



RN 159462-81-4 CAPLUS

CN Carbamic acid, [3-[2-[[(1,1-dimethylethyl)amino]carbonyl]-1-piperazinyl]-2-hydroxy-1-(phenylmethyl)propyl]-, tetrahydro-2-(1-methylethyl)-3-thienyl ester, [2R-[2α,3β[1S*,2R*(S*)]]]- (9CI) (CA INDEX NAME)

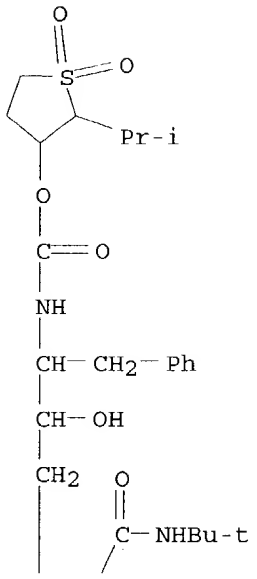
Absolute stereochemistry.



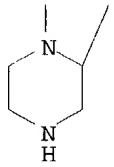
RN 159462-82-5 CAPLUS

CN Carbamic acid, [3-[2-[[(1,1-dimethylethyl)amino]carbonyl]-1-piperazinyl]-2-hydroxy-1-(phenylmethyl)propyl]-, tetrahydro-2-(1-methylethyl)-1,1-dioxido-3-thienyl ester, [2R-[2α,3β[1S*,2R*,3(S*)]]]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



AB A new hydroxyethylamine class of inhibitors was designed combining features from a clin. candidate, L-735524, along with small heterocyclic P2-ligands developed in these labs and their structure-activity relationship was studied.. Highly potent protease inhibitors possessing subnanomolar IC50's have been identified, which exhibit good antiviral potency against HIV-1 in cell culture. L-738872, a representative inhibitor in this class, showed 34% oral bioavailability in dogs.

L3 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1990:441332 CAPLUS
DN 113:41332
TI Preparation of peptide amides as human immunodeficiency virus inhibitors
IN Handa, Balraj Krishan; Machin, Peter James; Martin, Joseph Armstrong; Redshaw, Sally; Thomas, Gareth John
PA Hoffmann-La Roche, F., und Co. A.-G., Switz.
SO Eur. Pat. Appl., 69 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 346847	A2	19891220	EP 1989-110717	19890613
	EP 346847	A3	19911023		
	EP 346847	B1	19940511		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
				GB 1988-13940 A	19880613
				GB 1989-8035 A	19890410
	US 5157041	A	19921020	US 1989-362621	19890605
				GB 1988-13940 A	19880613
				GB 1989-8035 A	19890410
	ZA 8904285	A	19900228	ZA 1989-4285	19890606
				GB 1988-13940 A	19880613
	AU 8936130	A1	19891214	AU 1989-36130	19890607
	AU 624144	B2	19920604		
				GB 1988-13940 A	19880613
				GB 1989-8035 A	19890410
	HU 51254	A2	19900428	HU 1989-2903	19890607
	HU 205898	B	19920728		
				GB 1988-13940 A	19880613
				GB 1989-8035 A	19890410
	DK 8902863	A	19891214	DK 1989-2863	19890612
	DK 172747	B1	19990628		
				GB 1988-13940 A	19880613
				GB 1989-8035 A	19890410
	NO 8902407	A	19891214	NO 1989-2407	19890612
	NO 175715	B	19940815		
	NO 175715	C	19941123		
				GB 1988-13940 A	19880613
				GB 1989-8035 A	19890410
	JP 02042048	A2	19900213	JP 1989-149265	19890612
	JP 2515019	B2	19960710		
				GB 1988-13940 A	19880613
				GB 1989-8035 A	19890410
	KR 9705905	B1	19970422	KR 1989-8040	19890612
				GB 1988-13940 A	19880613
				GB 1989-8035 A	19890410
	FI 8902881	A	19891214	FI 1989-2881	19890613
	FI 95693	B	19951130		
	FI 95693	C	19960311		
				GB 1988-13940 A	19880613
				GB 1989-8035 A	19890410
	AT 105549	E	19940515	AT 1989-110717	19890613
				GB 1988-13940 A	19880613
				GB 1989-8035 A	19890410
				EP 1989-110717 A	19890613
	ES 2052815	T3	19940716	ES 1989-110717	19890613
				GB 1988-13940 A	19880613
				GB 1989-8035 A	19890410
	US 5446161	A	19950829	US 1992-916812	19920720
				GB 1988-13940 A	19880613
				GB 1989-8035 A	19890410
				US 1989-362621 A3	19890605
	US 5554756	A	19960910	US 1995-391380	19950217
				GB 1988-13940 A	19880613
				GB 1989-8035 A	19890410
				US 1989-362621 A3	19890605
				US 1992-916812 A3	19920720
	US 5652369	A	19970729	US 1995-394523	19950406

				GB 1988-13940 A 19880613
				GB 1989-8035 A 19890410
				US 1989-362621 A319890605
				US 1992-916812 A319920720
	US 5620987	A	19970415	US 1995-398478 19950410
				GB 1988-13940 A 19880613
				GB 1989-8035 A 19890410
				US 1989-362621 A319890605
				US 1992-916812 A319920720

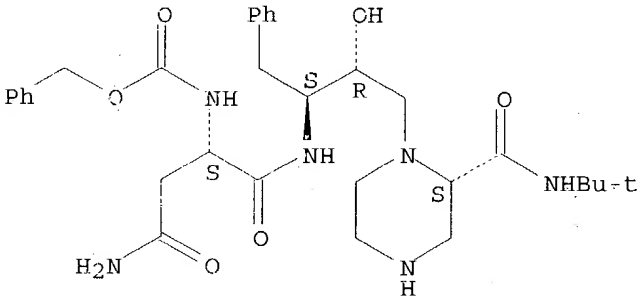
OS MARPAT 113:41332

IT **128019-64-7P 128111-43-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as HIV protease inhibitor)

RN 128019-64-7 CAPLUS

CN Carbamic acid, [3-amino-1-[[[3-[2-[[(1,1-dimethylethyl)amino]carbonyl]-1-piperazinyl]-2-hydroxy-1-(phenylmethyl)propyl]amino]carbonyl]-3-oxopropyl]-, phenylmethyl ester, monohydrochloride, [2S-[1[1R*(R*),2S*],2R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

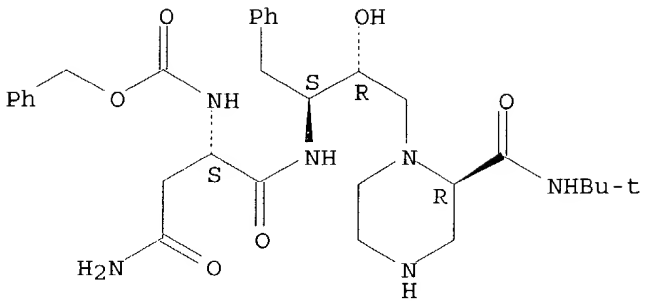


● HCl

RN 128111-43-3 CAPLUS

CN Carbamic acid, [3-amino-1-[[[3-[2-[[(1,1-dimethylethyl)amino]carbonyl]-1-piperazinyl]-2-hydroxy-1-(phenylmethyl)propyl]amino]carbonyl]-3-oxopropyl]-, phenylmethyl ester, monohydrochloride, [2R-[1[1S*(S*),2R*],2R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

AB R1R2NCHR3CONHCHR4CR5R6CH2N(:O)nR7CHR8R9 [I; R1 = alkoxycarbonyl, aralkoxycarbonyl, (ar)alkanoyl, cycloalkylcarbonyl, aroyl, heterocyclylcarbonyl, alkylsulfonyl, etc.; R2 = H; R1R2N = cyclic aromatic imide; R3 = (cyclo)alkyl, (aryl)alkyl, aryl, heterocyclylalkyl, cyanoalkyl, etc; R4 = alkyl, cycloalkyl(alkyl), aryl(alkyl); R5 = H; R6 = OH; R5R6 = :O; R7R8 = (un)substituted (CH2)3, (CH2)4, with 1 CH2 optionally replaced by NH, N(acyl), S, etc., optionally carrying 1 fused cycloalkane or (hetero)aromatic ring; R9 = alkoxycarbonyl, monoalkylcarbamoyl, CONHCHR10CONHR11; R10, R11 = alkyl; n = 0, 1] and their pharmaceutically acceptable salts were prepared, e.g., by coupling amines H2NCHR4CR5R6CH2NR7CHR8R9 with acids R1R2NCHR3CO2H. Thus, N1-isobutyl-L-isoleucylamide (preparation given) was coupled with Z-proline succinimide ester (Z = benzyloxycarbonyl), the resulting dipeptide was deprotected and coupled with (Z-phenylalanyl)methyl bromide, the intermediate tripeptide reduced by NaBH4 in EtOH, deprotected, and coupled with Z-Asn-OH to give N2-[N-[3(S)-[(Z-asparaginyl)amino]-2(R,S)-hydroxy-4-phenylbutyl]-L-prolyl]-N1-isobutyl-L-isoleucylamide. One (unspecified) of 2 isomers of the latter in vitro inhibited human immunodeficiency virus protease with an IC50 of 0.13 μM. IC50 values reported for 7 other I ranged from 0.01-0.87 μM.

=>

=> s alzheimer and piperazine
L4 234 ALZHEIMER AND PIPERAZINE

=> d his

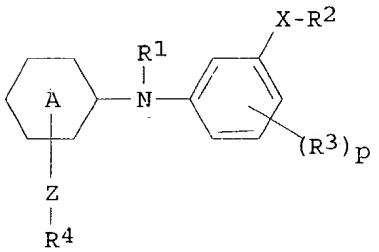
(FILE 'HOME' ENTERED AT 13:25:08 ON 28 FEB 2004)

FILE 'REGISTRY' ENTERED AT 13:25:18 ON 28 FEB 2004
L1 STRUCTURE UPLOADED
L2 10 S L1 SSS FULL

FILE 'CAPLUS' ENTERED AT 13:25:57 ON 28 FEB 2004
L3 8 S L2
L4 234 S ALZHEIMER AND PIPERAZINE

=> s l3 and l4
L5 0 L3 AND L4

```
=> s l4 and preventing
L6          14 L4 AND PREVENTING

=> s l4 and prevention
L7          21 L4 AND PREVENTION

=> s l4 and prevention and preventing and disease
L8           4 L4 AND PREVENTION AND PREVENTING AND DISEASE

=> d l8 fbib hitstr abs total

L8   ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2003:356443  CAPLUS
DN   138:368916
TI   Preparation of heteroarylamines as glycogen synthase kinase 3beta
     inhibitors
IN   Freyne, Eddy Jean Edgard; Buijnsters, Peter Jacobus Johannes Antonius;
     Willems, Marc; Embrechts, Werner Constant Johan; Love, Christopher John;
     Janssen, Paul Adriaan Jan; Lewi, Paulus Joannes; Heeres, Jan; De Jonge,
     Marc Rene; Koymans, Lucien Maria Henricus; Vinkers, Hendrik Maarten; Van
     Aken Koen, Jeanne Alfons; Diels, Gaston Stanislas Marcella
PA   Janssen Pharmaceutica N.V., Belg.
SO   PCT Int. Appl., 88 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND  DATE          APPLICATION NO.  DATE
     ------------------  ----  --------      ---------------  --------
PI   WO 2003037891       A1    20030508      WO 2002-EP12077  20021029
     WO 2003037891       C1    20030904
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD,
             RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
             NE, SN, TD, TG
                                          EP 2001-204196 A 20011101
OS   MARPAT 138:368916
GI
```



I

AB This invention concerns compds. of formula (I), N-oxides, pharmaceutically acceptable addition salts, quaternary amines and stereochem. isomeric forms thereof [wherein ring A = pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl; R1 = H, aryl, formyl, C1-6 alkylcarbonyl, C1-6 alkyl, formyl-C1-6 alkyl, C1-6 alkyloxycarbonyl, C1-6 alkylcarbonyloxy, C1-6 alkyloxy-C1-6 alkylcarbonyl optionally substituted with C1-6 alkyloxycarbonyl; X, Z = a direct bond or a linker atom or group; R2 = H, each (un)substituted C1-10 alkyl, C2-10alkenyl, C2-10 alkynyl, or carbocycle or heterocycle group; R3 = H, HO, halo, each optionally substituted C1-6 alkyl, C1-6 alkenyl, or C2-6alkynyl, C1-6 alkyloxy, C1-6 alkylthio, C1-6 alkyloxycarbonyl, C1-6 alkylcarbonyloxy, CO2H, cyano, nitro, amino, mono- or di(C1-6 alkyl)amino, polyhalo-C1-6 alkyl, polyhalo-C1-6 alkyloxy, polyhalo-C1-6 alkylthio, R21, R21-C1-6 alkyl, R21O, R21S, R21CO, R21S(O)n, R21S(O)nNH, NHCHO, CONHNH2, R21CONH, C(:NH)R21, etc.; wherein n = 1,2; R21 = each (un)substituted saturated, partially saturated, or aromatic mono-, di-, or tricyclic carbocycle or heterocycle group; R4 = (un)substituted saturated, partially saturated, or aromatic mono-, di-, or tricyclic carbocycle or heterocycle provided that -X-R2 and/or R3 is other than hydrogen; p = 1-3]. These compds. are useful for the **prevention** or the treatment of **diseases** mediated through glycogen synthase kinase 3β (GSK3β) including bipolar disorder (in particular manic depression), diabetes, **Alzheimer**'s **disease**, leukopenia, FTDP-17 (fronto-temporal dementia associated with Parkinson's **disease**), cortico-basal degeneration, progressive supranuclear palsy, multiple system atrophy, Pick's **disease**, Niemann Pick's **disease** type C, dementia pugilistica, dementia with tangles only, dementia with tangles and calcification, Down syndrome, myotonic dystrophy, Parkinsonism-dementia complex of Guam, AIDS related dementia, postencephalic Parkinsonism, prion **diseases** with tangles, subacute sclerosing panencephalitis, frontal lobe degeneration (FLD), argyrophilic grains **disease**, subacute sclerotizing panencephalitis (SSPE) (late complication of viral infections in the central nervous system), inflammatory **diseases**, cancer, dermatol. disorders, neuronal damage, schizophrenia, and pain. Thus, a mixture of 0.002 mol 2-[(4-cyano-3-benzyloxyphenyl)amino]pyrimidine-4-carboxylic acid Et ester and 0.002 mol **piperazine** in 15 mL MeOH was stirred at room temperature for 1 day to give 0.32 g N-[2-[(4-cyano-3-benzyloxyphenyl)amino]pyrimidin-4-ylcarbonyl] **piperazine** (II). II and 2-(1,3-benzodioxol-5-ylamino)-4-(2,4,6-trimethylphenylamino)pyrimidine showed pIC50 of 5.53 and 5.30, resp., against GSK3β.

RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

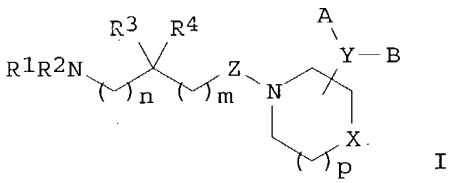
L8 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:977659 CAPLUS
DN 138:205081
TI Preparation of aminoacylpiperazines and -piperidines for promoting neuronal repair or **preventing** neuronal damage.
IN Lauffer, David; Tomlinson, Ronald; Ottow, Eckard; Botfield, Martyn
PA Vertex Pharmaceuticals Incorporated, USA
SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 2002102381 A1 20021227 WO 2002-US18999 20020613
WO 2002102381 C2 20030306
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2001-298328PP 20010614
US 2003191117 A1 20031009 US 2002-170965 20020613
US 2001-298328PP 20010614

OS MARPAT 138:205081

GI



I

AB Title compds. [I; R1-R4 = (O-, S-, SO-, SO2-, CO-, NR5-interrupted) alkyl, aralkyl, alkenyl, alkynyl, aralkenyl, aralkynyl; R1R2, R3R4 = atoms to form (aryl-fused) 4-7 membered rings; m, n = 0, 1; X = C(R5)2, NR5, N, O, S, SO, SO2; Y = bond, (O-, S-, SO-, SO2-, CO-, NR5-interrupted) alkyl, alkenyl, alkynyl; Z = CO, CH2; p = 0-2; A, B = H, aryl; 2 C atoms in the ring containing X and N may be linked via an alkylene or alkenylene moiety], were prepared Thus, N-benzyl-N-methylalanine, diisopropylethylamine, and pivaloyl chloride were stirred 2 h in CH2Cl2; 1-(4-fluorophenyl) **piperazine** in CH2Cl2 was added dropwise followed by stirring for 24 h to give 2-(benzylmethylamino)-1-[4-(4-fluorophenyl)-piperazin-1-yl]propan-1-one.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

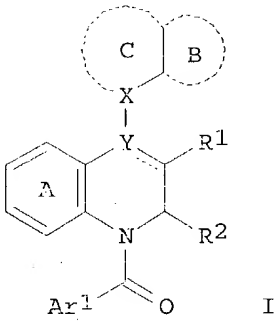
L8 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:849594 CAPLUS
DN 137:353065
TI Preparation of 4-heterocyclylquinoline derivatives as beta-amyloid precursor protein secretion promoters
IN Kakihana, Mitsuru; Kato, Kaneyoshi; Mori, Masaaki; Yamashita, Toshiro
PA Takeda Chemical Industries, Ltd., Japan
SO PCT Int. Appl., 233 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002088087	A1	20021107	WO 2002-JP4148	20020425

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
JP 2001-128677 A 20010426
JP 2002-43523 A 20020220
JP 2003313167 A2 20031106 JP 2002-124873 20020425
JP 2001-128677 A 20010426
JP 2002-43523 A 20020220
EP 1382598 A1 20040121 EP 2002-722787 20020425
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2001-128677 A 20010426
JP 2002-43523 A 20020220
WO 2002-JP4148 W 20020425

OS MARPAT 137:353065
GI



I

AB Novel compds. represented by the following general formula (I), salts thereof or prodrugs of the same [wherein R1, R2 = H, (un)substituted lower alkyl or HO; or R1 and R2 together with the C atom attached to them form a 4 to 7-membered ring; A1 = (un)substituted aromatic group; the ring A = (un)substituted benzene ring; the ring B = (un)substituted aromatic ring; the ring C = (un)substituted 4- to 8-membered ring which may be fused with an optionally substituted ring; X = CH or N; the solid line accompanied by a dotted line represents a single or double bond; when it represent a single bond, Y is CH or N; when it represents a double bond, it is C] are prepared These compds. provide soluble beta-amyloid precursor protein (soluble βAPP, sAPP) secretion promoters and/or apoptosis inhibitors which are efficacious in **preventing** and/or treating neurodegenerative **diseases** such as **Alzheimer**'s **disease**, Parkinson's **disease**, neuropathy, and senile dementia and nerve cell damages at cerebrovascular disorders. Thus, iodotrimethylsilane was added to a solution of cis-1-(3,4-dimethoxybenzoyl)-2-methyl-1,2,3,4-tetrahydro-4-quinolinol in CHCl3 under ice-cooling, stirred for 2 h, concentrated, dissolved in THF, and stirred with 1,2,3,4-tetrahydroquinoline and
BaCO3 at room temperature for 48 h to give cis-4-(1,2,3,4-tetrahydroquinolin-1-yl)-1-(3,4-dimethoxybenzoyl)-1,2,3,4-tetrahydroquinoline (II). II was separated by HPLC on a CHIRALPAK AD column to give (+)- and (-)-II. (-)-II at 10 nM increased the secretion of sAPP by .apprx.2.2 fold in rat

pheochromocytoma PC12h cell line and completely inhibited the apoptosis of PC12h cell caused by the glutamic acid-induced inhibition of the uptake of glutathione.

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:754196 CAPLUS
DN 137:257677
TI Methods of treating or **preventing Alzheimer**'s **disease** using 4-aryl-3-aralkoxypiperidines and -azabicyclooctanes
IN Nieman, James A.; Fang, Lawrence; Jagodzinska, Barbara
PA Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn Company
SO PCT Int. Appl., 449 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

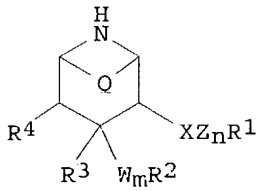
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002076440	A2	20021003	WO 2002-US9100	20020321
WO 2002076440	A3	20021128		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2001-278371PP 20010323
US 2001-308729PP 20010730

OS MARPAT 137:257677
GI



I

AB Disclosed are methods for treating or **preventing Alzheimer**'s **disease**, and other **diseases**, and/or inhibiting β-secretase enzyme, and/or inhibiting deposition of A beta peptide in a mammal, using 3,4-disubstituted piperidinyl compds. (I) wherein the variables R1, R2, R3, R4, Q, W, X, Z, m, and n are defined below. Although neither the compds. nor the methods of preparation are claimed, .apprx.150 example prepns., translations from the German examples of patent WO 9709311, are included. I inhibit β-secretase with IC50 < 50 μM; compds. that are effective inhibitors of β-secretase activity demonstrate reduced cleavage of the substrate as compared to a control. In I, R1 is aryl, heterocycle; R2 is Ph, naphthyl, acenaphthyl,

L Number	Hits	Search Text	DB	Time stamp
1	4037	("514/183,252.12,616,617").CCLS	USPAT	2004/02/28 13:48
2	1360	("544/358,398,402").CCLS	USPAT	2004/02/28 13:48
3	155	(("514/183,252.12,616,617").CCLS) and (("544/358,398,402").CCLS)	USPAT	2004/02/28 13:48
4	24	((("514/183,252.12,616,617").CCLS) and (("544/358,398,402").CCLS)) and Alzheimer	USPAT	2004/02/28 13:49

429

C:\APPS\EAST\bin\\default.wsp